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The authors of this study investigated parental smoking habits, pulmonary function capabilities, and nonspecific bronchial responsiveness to eucapneic hyperpnea with subfreezing air in a community-based sample of children and young adults.

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The Effect of Passive Smoking on Pulmonary Function and Nonspecific Bronchial Responsiveness in a Population-based Sample of Children and Young Adults[1-4]

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Introduction

Recent scientific investigations have observed adverse effects of parental cigarette smoking on level of pulmonary function (1) and rate of change of pulmonary function (2) in children. Whether passive smoking is an independent risk factor for these outcomes in children or whether the effects of passive smoking result from associations with other putative risk factors, such as respiratory infections (3, 4) or the occurrence of the atopic state (5), remains unclear. The association of parental cigarette smoking with wheezing symptoms in children (6, 7) as well as the identification of parental smoking as a factor that exacerbates the symptoms of childhood asthma (8) suggests a potential relationship between passive cigarette smoking and nonspecific bronchial responsiveness. To investigate this possibility, we studied parental cigarette smoking, pulmonary function, and nonspecific bronchial responsiveness to eucapneic hyperpnea with subfreezing air in a community-based sample of children and young adults.

Methods

Population

Details of the initial selection of the study population have been published previously (1). A random sample was selected from all children 5 to 9 yr of age in the public and parochial school systems of East Boston as of September 1974. These index children along with all members of their households constituted the initial study population. All members of the cohort have been screened on an annual basis since 1975, except for the second and third years when only index children were studied. Standardized questionnaires have been used to obtain information on respiratory symptoms and illnesses, smoking history, and demographic data. Parents answered for children 10 yr of age and younger, except for questions about the child's smoking history, which were asked during pulmonary function testing when the parents were not present. Asthma was defined as an affirmative response to a question about whether the subject has been told he or she has asthma by a doctor within the past 12 months. "Any wheeze" was defined as any category of affirmative response to a question about wheezing within the past 12 months. Episodes of dyspnea and wheeze were considered present if there was an affirmative response to a question about the occurrence of such episodes within the past 12 months. Current cigarette smoking was defined as currently smoking at least 1 cigarette per day or having quit such a habit within the past 12 months.

Pulmonary Function Testing

Subjects performed FVC maneuvers with the use of an 8-L, water-filled, portable, recording spirometer (Survey Spirometer; Warren Collins, Braintree, MA) while in the sitting position and without the use of noseclips; FVC, FEV_1, and FEF_{25-75} were measured using standard techniques. Mean values for the best of 3 of 5 acceptable tracings were used for analysis. All values were corrected to BTPS.

Cold Air Protocol

During the sixth through eighth interview cycles (1980 to 1982), a sample of the cohort families was selected to participate in a study of bronchial responsiveness to eucapneic hyperpnea with subfreezing air and allergy skin testing. An attempt was made to include as many subjects as possible who reported a history of asthma or wheezing, but asymptomatic subjects were selected randomly. If possible, the protocol was not performed within 3 wk of a respiratory infection, but this was not always achieved in the winter.

After completing the questionnaire and spirometry as described above, subjects performed eucapneic hyperpnea with subfreezing air using the technique of Deal and coworkers (9). Subjects hyperventilated with cold air for 4 min with a target minute ventilation of 25 times the initial FEV_1. Five minutes after completing cold air hypernea, repeat spirometry was performed. After completing the above protocol, each subject underwent allergy skin testing by the prick method. Four common environmental antigens were tested: mixed trees, mixed grasses, ragweed, and house dust. Atopy was defined as the occurrence of any wheal for at least one antigen.

Data Analysis

Response to cold air was evaluated by taking the difference between the prechallenge and postchallenge FEV_1 (ΔFEV_1). To correct for size, 2 analytic methods were employed. One method consisted of dividing ΔFEV_1 by predicted FEV_1 calculated from standard regression equations (10). Using predicted FEV_1 for this purpose offered several advantages. Predicted FEV_1 had a slightly higher correlation with ΔFEV_1 ($r = 0.36$) than did height ($r = 0.31$) or height[3] ($r = 0.33$). Use of predicted FEV_1 avoided size-correcting by a measure that itself may reflect bronchial tone, such as FVC or FEV_1. Finally, ΔFEV_1 as a percent of predicted FEV_1 is easily interpreted. The other method of size correction employed a linear regression model with ΔFEV_1 as the dependent variable and predicted FEV_1 along with exposure as the independent variables.

Chi-square test, *t* tests for independent samples, multiple linear regression, and stepwise

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TABLE 1

SUBJECTS STUDIED WITH AIR COMPARED WITH OTHER SUBJECTS IN THE POPULATION SAMPLE

	Subjects Year 6, 7, or 8 with Cold Air Data	Number	Subjects Year 6, 7, or 8 Without Cold Air Data	Number
Age, yr*	12.8 ± 0.2	292	12.9 ± 0.1	586
Current asthma, %	7.2†	292	3.9†	586
Any wheeze, %	18.9‡	291	12.3‡	586
Current personal smoking, %	7.9†	280	13.8†	552
Current maternal smoking, %	61.9	286	56.9	576
Current paternal smoking, %	43.1	274	48.2	562
FVC,, % pred*	101.3 ± 0.8	292	100.8 ± 0.7	409
FEV_1, % pred*	103.7 ± 0.8§	292	106.5 ± 0.8§	428
FEF_{25-75}, % pred*	92.6 ± 1.3§	292	97.4 ± 1.1§	409

* Values are mean ± SE.
† $p < 0.05$ by chi-square.
‡ $p < 0.01$ by chi-square.
§ $p < 0.02$ by t test for independent samples.

linear regression were performed using the Statistical Analysis System, Inc. software package (11). In regression models, discrete variables were assigned values of zero or 1 as follows: sex (1 = male), current personal smoking (1 = smoker), current maternal smoking (1 = smoking mother), current paternal smoking (1 = smoking father), atopy (1 = atopic), and history of cold within 2 wk (1 = yes). In the stepwise linear regression procedure a significance level of 0.15 was used for entry into and retention in the model, but statistical significance was considered to be present only for p values less than 0.05.

Results

Cold air challenge was performed by 292 subjects 6 to 21 yr of age during the study period. Characteristics of these subjects and the 586 similar-aged subjects not selected for the cold air protocol are given in table 1. By design, the prevalence of current asthma was greater among cold air subjects than among those not selected for cold air (7.2% versus 3.9%, respectively, $p < 0.05$). The FEV_1 percent predicted and FEF_{25-75} percent predicted were significantly lower in the cold air group, reflecting the preferential selection for the cold air protocol of subjects reporting wheeze. Personal smoking was significantly less common among cold air subjects than among subjects not chosen for cold air. Current maternal and paternal smoking did not differ significantly between the cold air group and the remainder of the population sample.

Wheezing symptoms reported by cold air subjects are given in table 2 for the 291 subjects with complete respiratory symptom data. Any wheeze and episodes of dyspnea and wheeze were reported by 14.1 and 3.0%, respectively, of subjects who denied current doctor-diagnosed asthma. Nineteen of the subjects denying current asthma had a history of previous doctor-diagnosed asthma. Current maternal smoking data were not available for 6 nonasthmatic subjects who underwent the cold air protocol, so these subjects were excluded from further analysis. Current paternal smoking data were available for 273 of the 286 subjects included in the analysis, including 20 of the 21 asthmatic subjects.

The characteristics of the subjects who underwent cold air challenge, stratified according to current asthma and current maternal smoking status, are given in table 3. Among the 265 subjects who denied current asthma, there were no differences between maternal smoking groups with respect to age, sex, or history of a cold within 2 wk. Among the 21 subjects with current asthma, children of smoking mothers had a lower mean age, were more often male, and had a higher frequency of recent colds, but these differences were not significant. Among nonasthmatics, children of smoking mothers were significantly more likely to smoke themselves than were children of nonsmoking mothers. None of the asthmatic subjects smoked themselves. Among nonasthmatics, atopy was significantly more common among children of smoking mothers than among those of nonsmoking mothers ($p = 0.02$). Among asthmatics, there was a similar trend.

Nonasthmatic subjects with smoking mothers had significantly lower mean percent predicted FEV_1 and FEF_{25-75} than did nonasthmatic subjects whose mothers denied smoking (table 3). Adjustment for personal smoking status using multiple regression did not alter the significant association between maternal smoking and low FEV_1 and FEF_{25-75} (results not shown). Among the asthmatic subjects, those with smoking mothers had lower mean FEV_1 and

TABLE 2

SYMPTOMS REPORTED BY COLD AIR SUBJECTS

	Subjects Denying Asthma		Subjects Reporting Asthma	
	(n)	(%)	(n)	(%)
Subjects	270		21	
Any wheeze	38	14.1	17	81.0
Episodes of dyspnea and wheeze	8	3.0	10	47.6

TABLE 3

SUBJECT CHARACTERISTICS

	Nonasthmatics		Asthmatics*	
	Nonsmoking Mother	Smoking Mother	Nonsmoking Mother	Smoking Mother
Subjects, n	97	168	12	9
Age, yr†	12.8 ± 0.3	12.9 ± 0.2	12.7 ± 0.9	11.0 ± 0.9
Males, %	51.6	49.4	50.0	77.8
Current smokers, %	3.1‡	11.3‡	0	0
> 1 possible allergy skin test, %	14.7‡ (n = 95)	27.2‡ (n = 162)	25.0	33.3
Cold within 2 wk, %	25.3 (n = 95)	25.3 (n = 166)	8.3	33.3
FVC, % pred†	102.8 ± 1.3§	99.7 ± 1.1§	104.0 ± 2.9	107.8 ± 3.8
FEV_1, % pred†	108.0 ± 1.4‖	101.4 ± 1.1‖	102.9 ± 3.5	100.8 ± 6.3
FEF_{25-75}, % pred† Mean ± SE	103.0 ± 2.3‖	88.2 ± 1.5‖	85.8 ± 6.8	76.1 ± 10.4

* None of the differences between maternal smoking groups are statistically significant for asthmatics.
† Values are mean ± SE.
‡ $p = 0.02$ by chi-square for difference between maternal smoking groups.
§ $0.05 < p < 0.10$ for difference between maternal smoking groups.
‖ $p < 0.001$ for difference between maternal smoking groups.

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TABLE 4

COLD AIR RESPONSIVENESS BY ASTHMA AND CURRENT MATERNAL SMOKING STATUS

Current Asthma Status	Current Maternal Smoking Status	Number	$\frac{\Delta FEV_1}{Pred.\ FEV_1} \times 100$*
Nonasthmatic	Nonsmoker	97	6.29 ± 0.67†
	Smoker	168	5.82 ± 0.43†
Asthmatic	Nonsmoker	12	11.9 ± 4.8‡
	Smoker	9	24.0 ± 3.3‡

* Values are mean ± SE.
† $p = 0.54$ for difference between maternal smoking categories.
‡ $p = 0.07$ for difference between maternal smoking categories.

TABLE 5

COLD AIR RESPONSIVENESS BY ASTHMA AND CURRENT PATERNAL SMOKING STATUS

Current Asthma Status	Current Paternal Smoking Status	Number	$\frac{\Delta FEV_1}{Pred.\ FEV_1} \times 100$*
Nonasthmatic	Nonsmoker	147	6.35 ± 0.52†
	Smoker	106	5.46 ± 0.58†
Asthmatic	Nonsmoker	11	17.1 ± 5.7†
	Smoker	9	15.0 ± 3.9†

* Values are mean ± SE.
† $p < 0.25$ for difference between paternal smoking categories

TABLE 6

MULTIPLE LINEAR REGRESSION RESULTS
DEPENDENT VARIABLE: CHANGE IN FEV_1 CAUSED BY HYPERNEA WITH COLD AIR

Group	Number	R^2	Independent Variable	Regression Coefficient	Standard Error	p Value
Nonasthmatics	265	0.15	Predicted FEV_1	0.079	0.011	0.0001
			Maternal smoking	−0.011	0.021	0.62
Asthmatics	21	0.71	Predicted FEV_1	0.515	0.079	0.0001
			Maternal smoking	0.319	0.125	0.02

TABLE 7

PULMONARY FUNCTION AND COLD AIR RESPONSE OF SUBJECTS DENYING ASTHMA AND WHEEZE

	Nonsmoking Mother	Smoking Mother
Subjects, n	87	139
FVC, % pred*	102.8 ± 1.4	100.9 ± 1.2
FEV_1, % pred*	106.1 ± 1.5†	103.0 ± 1.1†
FEF_{25-75}, % pred*	103.9 ± 2.4†	90.0 ± 1.5†
$\Delta FEV_1 \times 100$/predicted FEV_1*	6.31 ± 0.69	5.55 ± 0.47

* Values are mean ± SE.
† $p < 0.01$ for difference between maternal smoking groups.

FEF_{25-75} and higher mean FVC than did those with nonsmoking mothers, although these differences were not significant.

Among nonasthmatics, mean cold air response expressed as ΔFEV_1 divided by predicted FEV_1 did not differ between subjects with smoking and nonsmoking mothers (table 4). Among the 21 asthmatics there was a trend toward greater cold air response in subjects with smoking mothers than in those with nonsmoking mothers ($p = 0.07$). Cold air response was not significantly related to paternal smoking status for either nonasthmatics or asthmatics (table 5).

Using linear regression to adjust for predicted FEV_1, the regression coefficient for maternal smoking as a predictor of ΔFEV_1, did not differ significantly from zero among nonasthmatic subjects (table 6). For asthmatic subjects, the regression coefficient for maternal smoking was significantly different from zero ($p = 0.02$), indicating a significant relationship between maternal smoking and cold air response in this regression model.

Because of the possibility that some of the subjects who reported wheeze but denied doctor-diagnosed asthma may actually have had mild asthma that had not prompted them to seek medical attention, an analysis restricted to subjects who denied both asthma and wheeze was performed. As indicated in table 7, results were similar to those for all subjects denying asthma, i.e., maternal smoking was associated with significantly lower FEV_1 and FEF_{25-75} but not with any alteration of cold air response.

Stepwise multiple linear regression was performed to assess the relationship between cold air responsiveness and a number of variables of potential importance. Change in FEV_1 was used as the dependent variable. Predicted FEV_1 was entered as the first independent variable to correct for size. Other independent variables analyzed were age, sex, height, current personal smoking status, current maternal smoking status, current paternal smoking status, atopy, and history of a cold in the 2 wk prior to testing. Among nonasthmatics, no variable entered the model with a regression coefficient significantly different from zero after predicted FEV_1 was entered. Among the 21 asthmatic subjects, only current maternal smoking status entered the regression after predicted FEV_1. Current maternal smoking status remained a significant predictor of ΔFEV_1, and its regression coefficient changed only slightly when adjustment for history of a cold in the previous 2 wk was accomplished by forcing this variable into the model.

Discussion

Passive smoking by children of cigarette smokers has been found to be associated with decreased level of pulmonary function (1, 6, 12–15) although several studies have observed no effect of parental smoking on spirometric values (16–18). A longitudinal study of children and young adults observed a decreased rate of change of pulmonary function among subjects with smoking mothers (2), suggesting that passive smoking may have a deleterious effect on growth of the respiratory system. The mechanisms by which passive smoking may decrease the level or rate of change of pulmonary function have not been established.

A link between cigarette smoke exposure and increased bronchial respon-

siveness has been suggested by a number of physiologic investigations of adult subjects, although the relevance of these data to passive smoking in children is not certain. Active cigarette smoking has been shown to cause an acute increase in airway resistance in normal volunteers exposed in the laboratory (19, 20). A number of investigators have examined the influence of chronic cigarette smoking on bronchial responsiveness (21–28), and most (22–28) have found greater responsiveness among smokers than among nonsmokers.

The acute effects of passive smoking in adults have been studied in the laboratory with conflicting results. Dahms and coworkers (29) observed that asthmatic subjects, but not normal subjects, experienced a decline in pulmonary function after 1 h of exposure to sidestream cigarette smoke. Wiedemann and coworkers (30) and Shephard and colleagues (31), on the other hand, found that passive smoking caused no acute change in the pulmonary function of asthmatic subjects exposed in environmental chambers for 1 and 2 h, respectively. Wiedemann and coworkers (30) measured nonspecific bronchial reactivity to methacholine 1 day before and immediately after passive smoking in these same asthmatic subjects. They observed a small but significant decrease in responsiveness after passive smoking. Interpretation of these studies is difficult since the effects of autonomic nervous system responses to the stress of the in-chamber exposure were not taken into account. Furthermore, acute exposure studies may have little relevance to the effects of chronic exposure.

Population-based studies have provided conflicting evidence regarding the influence of passive smoking on nonspecific bronchial responsiveness and asthma among children. Dodge (7) found an association between parental smoking and symptoms of cough, phlegm, and wheeze among 676 Arizona school children 8 to 12 yr of age, although parental smoking was not related to level of pulmonary function. Weiss and coworkers (6) studied 650 children 5 to 9 yr of age in East Boston and found that parental cigarette smoking was associated with the report of persistant wheeze. Gortmaker and colleagues (32) analyzed data of 3,072 children between infancy and 17 yr of age from a random household health survey carried out in Michigan and Massachusetts. The diagnosis of asthma, based on reporting by the mother, was significantly more frequent among children with smoking mothers than among those whose mothers denied smoking. The investigators calculated that 18 to 34% of childhood asthma in their sample could be attributed to maternal smoking; however, the possibility of reporting bias in this study cannot be excluded. In contrast, Schenker and associates (3) studied 4,071 children 5 to 14 yr of age in rural Pennsylvania and found no association between parental smoking and either persistant wheeze or doctor-diagnosed asthma, although parental smoking was related to the occurrence of chest illnesses. Schilling and coworkers (17) found no association between parental smoking and respiratory symptoms among 816 children 7 yr of age and older in Connecticut and South Carolina.

In the present study, current maternal smoking was associated with significantly lower FEV_1 and FEF_{25-75} among the 265 subjects who denied recent doctor-diagnosed asthma. The magnitude of this effect was greater than that observed among our entire population (1, 6) and also exceeded that reported by other investigators who have observed significant effects of parental smoking on spirometric values (12–15). The preferential selection for cold air challenge of subjects reporting wheeze may have resulted in a sample displaying increased susceptibility to the effect of passive smoking on spirometric values, even among subjects denying recent asthma. A subject's report of recent medical therapy for asthma has been found to be a useful indicator of this disease (33), but there remains the possibility that some of the subjects who denied asthma actually had mild asthma that had not prompted them to seek medical attention. To eliminate potential error caused by misclassification of mild asthmatics as nonasthmatics, we performed an analysis restricted to subjects denying both asthma and wheeze and found results similar to those for all subjects denying asthma.

Despite the relationship between maternal smoking and pulmonary function, there was no association between maternal smoking and cold air responsiveness among subjects denying asthma. **These findings suggest that decreased pulmonary function associated with passive smoking is not due to increased nonspecific bronchial responsiveness. Instead, passive smoking may alter the growth of the immature respiratory system.**

If any relationship between passive smoking and nonspecific bronchial responsiveness does exist among nonasthmatic children and young adults, its demonstration may require more precise quantitation of passive smoke exposure. Household smoking reported on questionnaires correlates well with urinary cotinine as an indicator of passive smoke exposure (34, 35), but a more quantitative estimate of exposure based on cotinine measurements or detailed environmental data could enhance the investigation of passive smoking effects. **In addition, cold air challenge testing, which employs a single-dose stimulus and which measures response in terms of maximal expiratory spirometric values, may not be sufficiently sensitive to detect subtle physiologic changes induced by passive smoking among the nonasthmatic population.** Other physiologic techniques, such as bronchial provocation tests employing incremental doses of bronchoconstricting stimuli or partial expiratory flow-volume measurements, might improve sensitivity to such changes.

An important self-selection process also may serve to mask a relationship between passive smoking and bronchial responsiveness. Persons who are genetically predisposed to higher levels of bronchial responsiveness may tend to avoid smoking or to quit smoking once they start, whereas those who start and continue to smoke may be relatively less predisposed to the development of hyperresponsiveness. Because of this 'healthy smoker effect,' smoking families may be genetically inclined to lower responsiveness than nonsmoking families, obscuring any increase in bronchial responsiveness caused by active or passive cigarette smoking. **This may explain the lower prevalence of maternal smoking among asthmatic subjects than among nonasthmatic subjects in the present data.** Studies using longitudinal designs beginning in early childhood would be better able to shed light on these interrelationships, since bronchial responsiveness measured early in life could serve as a baseline, with subsequent examinations reflecting the effects of exposure. Cross-sectional data, such as presented in this report, should be interpreted with caution.

Among the 21 asthmatic subjects in the sample, maternal smoking was associated with higher mean FVC and lower mean FEV_1 and FEF_{25-75}, but these differences were not significant. Cold air responsiveness was greater among subjects with smoking mothers than among those with

nonsmoking mothers. Expressed as a percent of predicted FEV_1, the change in FEV_1 caused by eucapneic hyperpnea with subfreezing air was approximately twice as high among asthmatic children of smoking mothers as among those of nonsmoking mothers, a difference that was not significant ($p = 0.07$). In the linear regression analysis, maternal smoking was a significant ($p = 0.02$) predictor of ΔFEV_1 after adjusting for predicted FEV_1. In stepwise linear regression using change in FEV_1 as the dependent variable and predicted FEV_1 as the first independent variable, maternal smoking status was the only other independent variable that entered the model for the asthmatic subjects. The lack of a similar relationship between cold air response and paternal smoking may reflect less time spent at home or in close proximity to the children by fathers than by mothers.

Because our population-based sample contained a relatively small number of asthmatics, findings regarding the effects of passive smoking on young asthmatics should not be considered conclusive. Our data are in agreement with those of Murray and Morrison (36), who observed greater nonspecific bronchial responsiveness to histamine in association with maternal smoking among 94 asthmatic children. These data provide a physiologic basis for the retrospective findings of O'Connell and Logan (8), who reviewed the records of 400 asthmatics and found that parental smoking frequently exacerbated asthma symptoms, which often improved when parents stopped smoking.

In conclusion, among the 21 asthmatic [redacted] We were unable to demonstrate any effect of parental smoking on bronchial responsiveness among 265 similar-aged nonasthmatic subjects, despite the occurrence of [redacted] These findings suggest that lower levels of childhood pulmonary function associated with maternal smoking may not be due to increased bronchial responsiveness. Further research using more precise quantification of exposure and more comprehensive physiologic evaluation may help elucidate the effects of passive smoking during growth of the respiratory system.

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